

**In the Claims:**

Please cancel claims 1-22, without prejudice or disclaimer.

Please add the following new claims:

--23. A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

- a) introducing a molecular library of randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence, wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;
- b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and
- c) identifying said transdominant bioactive agent.

24. A method according to claim 23 wherein said identifying comprises:

- i) isolating said cell exhibiting an altered phenotype; and
- ii) isolating said nucleic acid encoding said transdominant bioactive agent.

25. A method according to claim 24 wherein said identifying further comprises:

- iii) sequencing said nucleic acid encoding said transdominant bioactive agent.

26. A method for in vitro screening for a molecule that binds a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

- a) introducing a molecular library of randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence, wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;

b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and  
c) identifying a target molecule to which said transdominant bioactive agent binds.

27. A method according to claim 26 wherein said identifying comprises:

- i) isolating said cell exhibiting an altered phenotype;
- ii) isolating said transdominant bioactive agent; and
- iii) binding said transdominant bioactive agent to said target.

28. A method according to claim 23 or claim 26 further comprising the step:

- d) isolating a target molecule using
  - i) said candidate nucleic acid; or
  - ii) the expression product of said candidate nucleic acid.

29. A method according to claim 23 or claim 26 wherein said nucleic acids further comprise a presentation sequence capable of presenting said expression product in a conformationally restricted form.

30. A method according to claim 23 or claim 26 wherein said introducing is with retroviral vectors.

31. A method according to claim 23 or claim 26 wherein said cells are mammalian cells.

32. A method according to claim 23 or claim 26 wherein said library comprises at least  $10^4$  different nucleic acids.

33. A method according to claim 23 or claim 26 wherein said library comprises at least  $10^5$  different nucleic acids.

34. A method according to claim 23 or claim 26 wherein said library comprises at least  $10^6$  different nucleic acids.

35. A method according to claim 23 or claim 26 wherein said library comprises at least  $10^7$  different nucleic acids.

36. A method according to claim 23 or claim 26 wherein said library comprises at least  $10^8$  different nucleic acids.

37. A method according to claim 23 or claim 26 wherein each of said candidate nucleic acids is linked to nucleic acid encoding at least one fusion partner.

38. A method according to claim 37 wherein said fusion partner is a presentation sequence capable of presenting said expression product in a conformationally restricted form.

39. A method according to claim 37 wherein said fusion partner is a rescue sequence.

40. A method according to claim 37 wherein said fusion partner is a stability sequence.

41. A method according to claim 37 wherein said fusion partner is a dimerization sequence.

42. A method according to claim 37 wherein said fusion partner is a targeting sequence.

43. A method according to claim 42 wherein said targeting sequence is selected from the group consisting of:

- a) a localizing signal sequence capable of constitutively localizing said translation product to a predetermined subcellular locale;
- b) a membrane-anchoring sequence capable of localizing said translation product to a cellular membrane; and

c) a secretory signal sequence capable of effecting the secretion of said translation product.

44. A method according to claim 43 wherein said targeting sequence is a nuclear localization signal (NLS).

45. A method according to claim 43 wherein said targeting sequence is a myristylation sequence.

46. A method for in vitro screening for a transdominant bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

- introducing a molecular library of randomized candidate nucleic acids into a first plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence;
- contacting said first plurality of cells with a second plurality of cells;
- screening said second plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and
- identifying said transdominant bioactive agent.

47. A method according to claim 46 wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized candidate peptides.

48. A method according to claim 47 wherein each of said candidate nucleic acids is linked to a nucleic acid encoding at least one fusion partner.

49. A method according to claim 48 wherein said fusion partner is a targeting sequence comprising a secretory signal sequence capable of effecting the secretion of said candidate peptides.

**Serial No.: 08/789,333**  
**Filed: January 23, 1997**

50. A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

*AM*

- a) introducing a molecular library of retroviral vectors comprising randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence and wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;
- b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and
- c) identifying said transdominant bioactive agent.